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THE AMERICAN
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VOL. 99 JULY, 1927 NO. 7

EDITORIAL

PRESENT STATUS OF THE OPIUM QUESTION

A FEW MONTHS ago the *British Medical Journal* expressed editorially the principal points that have developed in the effort to restrict the production and distribution of opium. The *Schweizerische Apotheker Zeitung* has recently republished this editorial in German and it will be worth while to set forth some of the points advanced.

A convention at The Hague in 1912 dealt with the question and formulated a number of regulations which were adopted by the representatives of many nations, but these agreements could not be effective until ratified formally by the legislative bodies of the nations themselves. Complete ratification was not secured.

A convention for further consideration of the question was held in 1925 at Geneva. Several definite restrictions were formulated, but the British Secretary of Foreign Affairs states that ten of the powers represented at this meeting have not ratified the agreements and, indeed, only the British Empire (exclusive of Canada and the Irish Free State) the Sudan and Portugal have done so. The president of the 1925 convention was enthusiastic as to its results, asserting that the agreements would be a means of effective regulation, would initiate a movement that would gain force from day to day and month to month and would give much force to the actions of The Hague Convention of 1912. These hopes have proved illusory. On all sides a contraband commerce in opium, morphine and cocaine is notoriously evident. The termination of exporting of opium from India is still ten years in the future. The critics of the Geneva Con-

vention assert that The Hague Convention represents no progress worth discussion, and that the decision of the later convention will remain a dead letter. One finds some indication of this in the remark of Sir Austin Chamberlain "that the convention of 1912 continues to be observed by the nations that have accepted it." It is opportune to remark that the American delegations at Geneva regarded the action of that convention as less saitsfactory on some points than that at The Hague and charged that some of the provisions thereof had not been fulfilled.

Recently, an Italian delegate to the League of Nations asserted that the 1925 convention was in some respects a retreat from that of 1912. If the earlier convention lacked the power to enforce its regulations it was largely due to the fact that the British Government had ordered its delegates to refuse all discussion on proposals to put the matter in the hands of an international commission to apply an international agreement.

The situation is unsatisfactory, and can be regarded with equanimity only by those who profit by the commerce in narcotics or by those who refuse to limit the use of the drugs to legitimate practice.

A new development has just occurred which promises to give, at least, a positive character to the discussions in the Opium Committee. Backed by a suggestion (perhaps, one may say orders) of "Il Duce," an Italian delegate has demanded and secured membership in the committee and has begun at once to urge more definite action. Italy claimed membership because it produces no opium or derivatives and it was properly asserted that the committee should not be made up entirely of those that represent interests. A resolution introduced by the Italian delegate providing for certain actions was defeated by a vote of 7 to 2, the Italian and Siam delegates alone voting for it, but the conditions seem favorable for some positive action and especially for compelling some of the interested nations to show their hands.

HENRY LEFFMANN.

ORIGINAL ARTICLES

GRADUATION ADDRESS*

By Dr. Edgar Fahs Smith

IN MY OFFICE hangs a beautiful steel engraving, a portrait of Matthew Goeffroy—Master of Pharmacy—Master of Pharmacy! More than two centuries ago Matthew Goeffroy lived and moved in that attractive and wonderful city of Paris, where he practiced your profession. Many times have my eyes rested upon this delineation of his intelligent and noble countenance, and on all occasions it has seemed to me to breathe out happiness and genuine profundity of thought.

Visitors to my office, whose eyes have chanced to observe this picture, have asked me why I pay such particular attention to it—because, they say, it represents merely a "Master of Pharmacy." Well, my invariable answer to such inquiries has been, "Let me tell you his story"—and this is what I want you to heed. Then, as I proceeded with a description of his laboratory, of his library and of his wonderful collections it rapidly dawned upon my auditors that this particular individual had tapped every source of human knowledge and, thus engaged, had raised pharmacy itself to a most exalted plane.

Further, when I dwelt upon the atmosphere of Matthew Goeffroy's workshop and of his library—gradually, quietly introducing also his son, who was being reared under these grandest of educational influences, and to which he responded with all his native talents and youthful ardor, my visitors invariably became thoughtful, and marvelled on hearing that this son later contributed mightily to the growth and advancement not only of pharmacy and medicine but particularly to the development of chemistry, and that his rich contributions came as the result of the broadest training which it had been possible for him to receive—because the Master of Pharmacy, his father, Matthew Goeffroy, assiduously brought into that pharmacy of his, into his workshop, into his library the greatest scientific and literary characters of the day.

*Given at the Commencement Day Exercises, Philadelphia College of Pharmacy and Science, June, 1927.

One wonders at what Matthew Goeffroy considered, evidently, as a suitable training for his son, when one is told that thither, to that workshop, brought Cassini his astronomical instruments, Sebastian his machine models, Jablot his magnets, duVerney his charts in anatomy and that grand old man, Homberg, his chemical outfit. And the conferences held there in the home of Matthew Goeffroy became the model and foundation of the several courses of experiments which were later given in the colleges of Paris.

And the purpose of it all was what? That Matthew Goeffroy's son might be instructed—for he designed to bring him up into his own business, that is, into Pharmacy, and to leave behind him a worthy successor in his shop.

Mark, please, that patient and, at the same time, consuming desire of the father that the son should enjoy a *broad* training. And we may ask, "Why all this interest and effort? Why all this anxiety?" And the answer would be, "For the simple reason that Matthew Goeffroy believed and knew how large a share of knowledge was required to arrive at perfection in Pharmacy."

Before I knew better, there existed in my untutored intellect a suspicion that to be a pharmacist—or, as the world says, a druggist —didn't require *very* much knowledge; but here was a Master of Pharmacy, more than two hundred years ago, who was solicitous that the lad dear to him should have the noblest and best sort of training, and hence he was unwilling to omit any circumstance that might contribute to make him a *Master* in his profession, which the father had followed with so much advantage to himself both in point of pleasure and of profit.

And this unique old Master of Pharmacy arranged that that favorite son of his should go to Montpellier, to reside with another noted apothecary there, whose son he in turn took to Paris in exchange —that by this means these boys might become acquainted with the different methods of practice and be able to learn abroad that which might perhaps have escaped their notice at home.

Wasn't this virtually an exchange of students—a scheme in education which is much in mind in these days, and considered to be worth while? Yes, the Master of Pharmacy—Matthew Geoffroy—evidently thought so, and the results were admirable.

But now, for a brief moment, that you have heard of the evident conviction of Matthew Geoffroy—Master of Pharmacy—that your

profession, the profession into which you have been officially admitted within the hour, required and deserved the broadest preparatory training—now, I say, permit me to introduce that son for whose welfare and advantage the father was ever solicitous. He bore the name "Stephen Francis Goeffroy" and was born in 1672—long ago; but it was through his life, the life of Stephen, that I learned to know that old Master of Pharmacy, because the fundamental training advocated by the father sent the son into my particular field of science, chemistry, in which he wrought so gloriously.

Sir Isaac Newton, you all know, was truthfully, or truly, the father of the doctrine of chemical affinity—that is, the attraction between the smallest particles of matter; and until 1718 no one paid any particular attention to that. They talked about the law of gravitation and so forth. But in 1718 Stephen Goeffroy, out of the blue, set forth "A Table of the Affinities or Relations which Different Substances in Chemistry—(Particles of Barium Chloride, of Phosphate of Sodium) —Bear to Each Other," and it was the consequence of his thought on the idea of Sir Isaac Newton as to the attraction between the smallest particles of matter.

This table, or this scheme, of Stephen Goeffroy's occasioned much consternation among scientists, who were a bit apprehensive; but very soon they grew sensible, lost their scruples, and declared that Stephen Goeffroy's suggestions might well be admitted, if rightly understood, and if carried on to the utmost degree of exactness might well become a fundamental law for chemical operation. And today in tracing the doctrine of chemical affinity there is Sir Isaac Newton, first, and then comes Stephen Francis Goeffroy, an apothecary's son.

All that happened; and that last name cannot be omitted when scientists discuss the discoveries made in the field of chemistry. And may I ask you, this Class of 1927, to reflect on this story which I have told to you? Out of an apothecary's shop, where a Master of Pharmacy held sway, there came the benefits accruing from a broad fundamental preparation in his particular science, as well as the gift of a son who paid his tribute to another science in that he aided in laying one of the foundation stones in that science. Frequently, I sit and I look at these pictures, of father and son, and then I turn to the books

of Stephen to note how he told his thought to the scientific world. And then I say, "He was a druggist. He was a pharmacist. He is an example for all of them who follow his footsteps, endeavoring to do as he did."

Now, I wonder if you folks have read that delightful, charming and wonderful book—it appeared only recently—that bears the arresting title "Four Thousand Years of Pharmacy"? It was written by one whom you all know, one of your professors—I will not mention his name, that is, to the Class, but will mention it to the audience, to the listeners-in;—it was written by Dr. LaWall. It is indeed a remarkable contribution. Read it—if you have not already done so. Become acquainted with some of those noble pharmacists who have preceded you. Their efforts, their work will inspire you as nothing else will as to the dignity of your profession.

There is one person mentioned in that book whose life was a real tragedy. Like Goeffroy, he was an apothecary indeed; and he died in his apothecary shop in Köping, Sweden. His name was Carl Wilhelm Scheele. All of you have seen his picture. Pharmaceutical and chemical literature of the most recent day is eager to tell the world about Scheele—for in his apothecary shop, in his drug store, he did, between times and after hours, such epoch-making things as the discovering of chlorine—little dreaming what that element would do in the hands of his successor—barium, cream of tartar, phosphoric acid, lactic acid, glycerine, citric, malic, gallic, oxalic, uric and mucic acid, and hundreds of other important things which we have and use today. Carl Scheele, an apothecary, working between times and after hours—not frequenting movies nor taking joy rides, just working, was responsible for all these offerings, wonderful as they are, that he made and gave to the world; and it all was a consequence of his being a Master in Pharmacy—pursuing the advice and following the example of old Matthew Goeffroy.

A fortnight ago a medical doctor, living now where Scheele lived in the days of his great experimental activity, wrote me pleadingly for a photograph, just a photograph, of an autograph letter of Carl W. Scheele's—imagining I could do this because I had given him an autograph of Henricus Cornelius Agrippa, an old alchemist of 1530.

I could do that, but I could not give him a photograph of a letter written by Carl Scheele.

But the real works of Carl Scheele are with us today, and we can never estimate the great value to humanity and civilization bestowed by this unassuming apothecary, this Master of Pharmacy. Whenever you get a chance, let your eyes linger on his attractive, intelligent countenance and pray God that his spirit, in a measure, may be yours.

When, in 1817, John Gorham assumed the chair of chemistry in Harvard University, President John Adams—our second President —wrote him, and in that letter, among other things, said: "Consider the odor of the apple, the odor of the quince, that of the orange, that of the pineapple, that of the roses, that of the lilies, and so forth. What are they?" An elder brother of yours in Pharmacy, an alumnus of this College of Pharmacy and Science, lived and answered those interrogatories. I allude to Dr. Frederick B. Power, who very recently, after the attainment of a high place in science throughout all the world, passed on to the Great Beyond. He, too, was a Master of Pharmacy.

What a glorious heritage, Class of 1927, is indeed yours! You may well glory in it. The great Masters of Pharmacy may easily become known to you! They comprehended the dignity and the profoundness of your science and profession, and would have you follow them. Think of the happiness, comfort and joy, and the contribution to welfare, that their labors conferred on their fellow men; and remember that they are bidding you to do likewise.

Every drug shop, back of its curtained ante-room, should have a laboratory or a space where the presiding genii are the spirits of those departed Masters of Pharmacy whispering welcome to you and telling you of the secrets to which they will lead you if untiringly, devoutly and prayerfully you will follow in their footsteps. And then, when a stupendous volume entitled "Five Thousand Years of Pharmacy" makes its appearance in the far, far future, your names will be writ high upon its pages, for you will have held a foremost place "among the swift runners who hand over the lamp of life and transmit from one generation to another the fire kindled, in the childhood of the world, at the Promethean altar of science." Farewell.

DIGITONIN—ITS PROPERTIES, ISOLATION AND QUANTITATIVE DETERMINATION*

By I. S. Mellanoff, Ph.G., B.Sc.

Introduction

THIS INVESTIGATION was instituted with the object of finding a chemical process for the isolation and quantitative determination of Digitonin. This substance is found with other active principles in the seeds and leaves of Digitalis purpurea, and probably in other species of digitalis containing heart-stimulating principles. It is also found in commercial preparations made from parts of the above-mentioned plants. Reagents were sought that would not have destructive effects and yet have the property to precipitate Digitonin as a specific substance, and be so constituted that its excess could be easily removed.

General Characteristics of Digitonin

Digitonin[1] has the chemical composition C_{54} H_{92} O_{28} or C_{55} H_{94} O_{28} and belongs to the group of saponins. It is either crystalline or amorphous depending upon the solution from which it is obtained. It completely melts at 235° C. but starts to soften at 225° C. It is soluble in 600 parts of cold and 50 parts of warm water to a turbid solution which froths on agitation. It is less soluble when pure but dissolves readily when present with some of the other principles. The aqueous solution is lævorotatory $[a]_D$ 49.25°. It is slightly soluble in absolute alcohol but dissolves to a clear solution in 50 parts of 50% alcohol. It is practically insoluble in ether, chloroform or petroleum ether. It forms crystalline addition compounds with many substances.

The aqueous solution yields a gummy mass on evaporation. All my attempts to crystallize Digitonin from water were unsuccessful. It is completely precipitated by adding ether to an alcoholic solution. This precipitate is in the form of slender crystalline needles containing alcohol and water of crystallization. It is soluble in 10 parts of

*This paper represents work conducted under a research grant from the F. B. Kilmer Fellowship at the Philadelphia College of Pharmacy and Science, and under the supervision of Dr. Arno Viehoever, Professor of Biology and Pharmacognosy.

85% alcohol and if the solution is kept at 45° C. from six to eight hours, the greater part of the Digitonin will crystallize out.

Digitonin was obtained by Schmiedeberg [2] in an amorphous form, while Kiliani obtained the same in a crystalline form. No doubt the former in trying to isolate Digitonin used an aqueous solution, while the latter used an alcohol or ether-alcohol solution. The author was able to get it in both forms using the above solvents.

Barium hydroxide [3] and basic lead acetate will precipitate Digitonin forming barium saponate and lead saponate respectively. Tannic acid precipitates it from an aqueous solution. It is hydrolyzed by heating with alcoholic hydrochloric acid to dextrose (2 molecules), galactose (2 molecules), and digitogenin ($C_{30}H_{48}O_6$ or $C_{31}H_{50}O_6$). The split product is crystalline and will soften at 240° C. It is thought there is also formed an amorphous substance called digitsaponin.

By the addition of amyl alcohol to a hot aqueous solution of digitonin, a crystalline precipitate is obtained containing amyl alcohol and water of crystallization. Similar crystalline compounds of digitonin with other alcohols and with phenols have been described by T. Houdas.[4] A number of these were obtained in the present investigation.

Digitonin gives the characteristic saponin reaction. It will dissolve in sulphuric acid with a red color and the color is intensified by the addition of bromine water. Sulphuric acid (50%) produces a yellow color in the cold which changes to red and finally to black on heating. Concentrated hydrochloric acid gives a yellowish color on standing or heating, then a violet-red with a slight greenish fluorescence.

Deichard [5] has found that if an evaporated solution of cobalt nitrate is rubbed with digitonin and glacial acetic acid and allowed to stand from twenty-four to thirty-six hours, rose-red transparent hexagonal crystals are formed.

Digitonin has the property of forming addition compounds with cholesterol, phytosterol, alpha-naphthol, beta-naphthol, para-bromo-naphthol, thiophenol, carvomenthol, l-alpha-terpineol, d-alpha-terpineol, ac-tetra-hydro-beta-naphthol, alpha-phenylethyl alcohol, sec. octyl alcohol, butyl alcohol, amyl alcohol, geraniol, lianeol, phenol, propyl and iso-propyl alcohol and para-bromo-phenol. All of these compounds are fairly insoluble and the amount of water of crystallization in each case is somewhat variable. When the addition com-

pound is extracted with hot water, benzene or xylene, it is broken down into its component parts. This reaction takes place with different degrees of rapidity.

Quantitative Determination of Digitonin [6]

(1) *Digitonin-cholesterol Method.*—One molecule of digitonin combines with one molecule of cholesterol to form an addition compound. If the approximate amount of digitonin is known, the amount of cholesterol to be used can be calculated from their molecular ratio. A small excess of cholesterol is added to insure complete precipitation. If the amount of digitonin is not known, then, small amounts of cholesterol are added until complete precipitation. To a hot solution of digitonin in 90% alcohol is added a hot solution of cholesterol (1% of cholesterol in 90% alcohol) in excess. The mixture is then allowed to stand from twelve to twenty-four hours. Precipitation did not require from twelve to twenty-four hours but was included because it was most convenient. The precipitate is then filtered off by means of a gooch crucible and washed with 90% alcohol. The filtrate is then treated with more cholesterol, by the above method, to insure complete precipitation. The precipitate is dried in a desiccator over sulphuric acid. The crystals are needle shape and arrange themselves like the spokes of a wheel about an axis. In all calculations the molecular weight for digitonin was taken as C_{55} H_{94} O_{28} (1202) and Cholesterol C_{27} H_{45} OH (386).

Digitonin-cholesterol.... C_{55} H_{94} O_{28} — C_{27} H_{45} OH (1588)

$\frac{1202}{1588} = .757$ (factor for changing the weight of digitonin-cholesterol to digitonin).

$$\frac{\text{Wt. of digitonin-cholesterol} \times .757 \times 100}{\text{Wt. of samples taken}} = \% \text{ digitonin.}$$

Digitonin-cholesterol molecule can be split up into its component parts by extraction with hot xylene.

(2) *Digitonin-alpha-naphthol Method.*—Digitonin and alpha-naphthol combine in molecular ratio to form an addition compound that will crystallize out of solution with eight (8) molecules of water. To a hot solution of digitonin in 20% alcohol is added an excess of alpha-naphthol (0.5% alpha-naphthol in 20% alcohol). On cooling needle shape crystals of digitonin-alpha-naphthol will separate which

are difficult to filter. These are filtered by means of a gooch crucible and washed with 20% alcohol and dried in a desiccator over sulphuric acid. The filtrate is then treated with more alpha-naphthol to insure complete precipitation. The addition compound is soluble in 90% alcohol and in hot water but sparingly in cold. The alpha-naphthol can be separated from the union by the extraction with boiling benzene, and can be sublimed by heating in a high vacuum to 150° C. The addition compound will turn pink upon standing. (According to Dr. Henry Leffmann alpha-naphthol will turn pink upon standing, so that this fact is of no diagnostic value.)

Digitonin-alpha-naphthol $C_{55}\ H_{94}\ O_{28} - C_{10}\ H_7\ OH.\ 8H_2O$ (1490)

$\frac{1202}{1490} = .8067$ (factor for changing the weight of digitonin-alpha-naphthol to digitonin).

$$\frac{\text{Wt. of digitonin-alpha-naphthol} \times .8068 \times 100}{\text{Wt. of sample}} = \%\ \text{digitonin.}$$

(3) *Digitonin-beta-naphthol Method.*—This method is carried out exactly like the alpha-naphthol method only using beta-naphthol instead. The crystalline compound formed contains 10 molecules of water. Solvents have the same action upon it. This addition compound will not turn pink.

Digitonin-beta-naphthol $C_{55}\ H_{94}\ O_{28} - C_{10}\ H_7\ OH.10\ H_2O$ (1526)

$\frac{1202}{1526} = .7877$ (factor for changing the weight of digitonin-beta-naphthol to digitonin).

$$\frac{\text{Wt. of digitonin-beta-naphthol} \times .7877 \times 100}{\text{Wt. of sample}} = \%\ \text{digitonin.}$$

(4) *Digitonin-beta-naphthol Method.*—Bromo-beta-naphthol and digitonin will unite in molecular ratio to form an addition compound which will crystallize out of solution with eight molecules of water. To a hot solution of digitonin in 25% hot alcohol, is added a hot solution of bromo-beta-naphthol (1% of bromo-beta-naphthol in 25% alcohol). Upon cooling the addition compound will crystallize out in fine needles. Filter upon a gooch crucible and wash with 25% alcohol and dry in a desiccator. To insure complete precipitation more bromo-beta-naphthol is added. The addition compound is insoluble

in cold water, slightly soluble in hot water and in alcohol. Steam decomposes it slowly.

Digitonin-bromo-beta-naphthol..... $C_{55}\ H_{94}\ O_{28} - C_{10}\ H_7\ Br\ OH.\ 8H_2O$ (1579)

$\frac{1202}{1579} = .7612$ (factor for changing the weight of digitonin-bromo-beta-naphthol to digitonin).

$$\frac{\text{Wt. of digitonin-bromo-beta-naphthol} \times .7612 \times 100}{\text{Wt. of sample}} = \%\ \text{digitonin.}$$

(5) *Digitonin-terpineol Method.*—Terpineol (1% in 30% alcohol) and digitonin in a hot solution of 30% alcohol will combine in molecular ratio to form an addition compound. Upon cooling needle-shape crystals will separate out of solution. They are filtered off upon a gooch crucible and dried in a desiccator. They are insoluble in cold water but difficultly soluble in hot water and very soluble in alcohol, and slightly decomposed with ether and benzene and completely with boiling xylene. The addition compound will crystallize out of solution with six (6) molecules of water.

Digitonin-terpineol..... $C_{55}\ H_{94}\ O_{28}\ C_{10}\ H_{18}\ O.\ 6H_2O$ (1464)

$\frac{1202}{1464} = .8204$ (factor for changing wt. of digitonin-terpineol to digitonin).

$$\frac{\text{Wt. of digitonin-terpineol} \times .8204 \times 100}{\text{Wt. of sample}} = \%\ \text{digitonin.}$$

(6) *Digitonin-thiophenol Method.*—Digitonin and thiophenol will combine in molecular ratio in a cold solution. Thiophenol (0.25% in 30% alcohol) is mixed with a solution of digitonin in 30% alcohol and allowed to stand until crystallization takes place. The separated complex compound is filtered off and washed with 20% alcohol, then dried in a desiccator over sulphuric acid. It has on odor of thiophenol and is quite soluble in water. Boiling with ether will remove the thiophenol. It is thought that the addition compound will crystallize out of solution with six (6) molecules of water, however, this is doubtful.

Digitonin-thiophenol.... $C_{55}\ H_{94}\ O_{28}\ C_6\ H_5\ SH.\ 6H_2O$ (1420)

$\frac{1202}{1420}$=.8466 (factor for changing the weight of digitonin-thiophenol to digitonin).

$$\frac{\text{Wt. of digitonin-thiophenol} \times .8466 \times 100}{\text{Wt. of sample}} = \% \text{ digitonin.}$$

The following tables show the digitonin content of Digitalin (Merck) and Digitonin (Merck), using the methods described above:

TABLE I

DIGITONIN-CHOLESTEROL METHOD

Weight of Digitalin (Merck)	*Weight of Digitonin-cholesterol*	*Per cent. of Digitonin*
0.1694 gm.	0.0702	31.39
" "	0.0698	31.21
" "	0.0686	30.63
" "	0.0700	31.30
0.1894 gm.	0.0770	30.78
" "	0.0772	30.86
" "	0.0771	30.82
" "	0.0768	30.70
" "	0.0775	31.98
0.0847 gm.	0.0362	32.36
" "	0.0337	30.12
" "	0.0338	30.21
" "	0.0344	30.73
" "	0.0363	32.45
" "	0.0343	30.63
" "	0.0341	30.48
" "	0.0364	32.54
" "	0.0350	31.30
" "	0.0361	32.27
" "	0.0352	31.46
" "	0.0349	31.21
" "	0.0351	31.39
	Average	31.10

Weight of Digitonin (Merck)		
0.0377 gm.	0.0413	82.9
" "	0.0415	83.3
" "	0.0417	83.7
" "	0.0414	83.1
" "	0.0415	83.3
" "	0.0412	82.7
	Average	83.3

TABLE II

DIGITONIN-BETA-NAPHTHOL METHOD

Weight of Digitalin (Merck)	*Weight of Digitonin-beta-naphthol*	*Per cent. of Digitonin*
0.0947 gm.	0.0347 gm.	28.9
" "	0.0348	28.9
" "	0.0349	30.0
" "	0.0341	28.3
" "	0.0354	29.4
" "	0.0346	28.8
" "	0.0328	27.3
" "	0.0357	29.7
" "	0.0331	27.6
" "	0.0345	28.7
0.1894 gm.	0.0691	28.7
" "	0.0692	28.8
" "	0.0656	27.3
" "	0.0694	28.9
" "	0.0682	28.3
	Average	28.6

Weight of Digitalin (Merck)		*Weight of Digitonin-beta-naphthol*	*Per cent. of Digitonin*
0.0377 gm.	Digitonin	0.0379	79.3
" "	(Merck)	0.0386	80.6
" "		0.0381	79.6
" "		0.0377	78.9
" "		0.0378	79.1
		Average	79.5

TABLE III

DIGITONIN-ALPHA-NAPHTHOL METHOD

Weight of Digitalin (Merck)		*Weight of Digitonin-alpha-naphthol*	*Per cent. of Digitonin*
0.2 gm.		0.0682 gm.	27.5
" "		0.0687	27.7
" "		0.0691	27.8
" "		0.0700	28.2
" "		0.0712	28.7
		Average	28.00
0.03087 gm.	Digitonin	0.0315	82.3
" "	(Merck)	0.0307	80.3
" "		0.0311	81.3
" "		0.0305	79.7
" "		0.0308	80.5
		Average	80.8

TABLE IV

DIGITONIN-THIOPHENOL METHOD

Weight of Digitalin (Merck)	*Weight of Digitonin-thiophenol*	*Per cent. of Digitonin*
0.2 gm. Digitalin	0.0527 gm.	22.3
" " (Merck)	0.0502	21.2
" "	0.0510	21.6
" "	0.0506	21.4
" "	0.0516	21.8
	Average	21.7
0.015435 gm. Digitonin	0.0123	67.4
" " (Merck)	0.0126	69.1
" "	0.0122	66.9
" "	0.0122	66.9
" "	0.0121	66.3
	Average	67.3

TABLE V

DIGITONIN-TERPINEOL METHOD

Weight of Sample	*Weight of Digitonin-terpineol*	*Per cent. of Digitonin*
0.2 gm. Digitalin	0.0683 gm.	28.0
" " (Merck)	0.0692	28.4
" "	0.0687	28.2
" "	0.0683	28.0
" "	0.0691	28.4
" "	0.0682	28.0
" "	0.0680	27.9
" "	0.0677	27.9
	Average	28.1

Weight of Sample	*Weight of Digitonin-terpineol*	*Per cent. of Digitonin*
0.015435 gm. Digitonin	0.0144	75.4
" " (Merck)	0.0147	77.0
" "	0.0143	74.9
" "	0.0143	74.9
" "	0.0144	75.4
	Average	75.5

TABLE VI

DIGITONIN-BROMO-NAPHTHOL METHOD

Weight of Sample	*Weight of Digitonin-bromo-naphthol*	*Per cent. of Digitonin*
0.2 gm. Digitalin	0.0752 gm.	28.6
" " (Merck)	0.0772	29.4
" "	0.0758	28.8
" "	0.0754	28.7
" "	0.0761	28.9
" "	0.0763	29.0
" "	0.0730	27.8
" "	0.0742	28.2
" "	0.0747	28.4
" "	0.0744	28.3
	Average	28.6
0.03087 gm. Digitonin	0.0330	81.3
" " (Merck)	0.0333	82.1
" "	0.0328	80.8
" "	0.0331	81.1
" "	0.0326	80.3
	Average	81.1

DIGITONIN CONTENT OF THE SEEDS OF DIGITALIS PURPUREA BY THE DIGITONIN-CHOLESTEROL METHOD

Weight of Seeds	*Weight of Digitonin-cholesterol*	*Per cent. of Digitonin*
1.25 gm.	0.0226	1.36
" "	0.0227	1.38
" "	0.0226	1.36
" "	0.0246	1.49
" "	0.0231	1.40
" "	0.0234	1.42
" "	0.0240	1.45
2.5 gm.	0.0457	1.38
" "	0.0463	1.40
" "	0.0456	1.38
" "	0.0462	1.40
" "	0.0470	1.42
" "	0.0471	1.43
	Average	1.40

Extraction of Seeds of Digitalis Purpurea

The seeds were placed in a container and covered with a stratum of petroleum ether and allowed to macerate for two-three hours. They were taken out and dried, then subjected to a coarse milling. Following this treatment, they were macerated for a second time. After the second maceration with petroleum ether for the fatty matter, the seeds were milled until the powder passed through a No. 60 sieve. The powder was placed in a percolator and extracted with petroleum ether until a few drops of the percolate evaporated from a filter paper left no greasy stain. The powder was removed from the percolator and exposed to the air until the odor of the solvent was no longer noticeable. It was then moistened with an alcohol-water menstruum (1-1) transferred to a percolator, packed loosely, and enough menstruum added to saturate the powder and leave a stratum above it. When the liquid began to drop from the percolator, the

lower orifice was closed and the powder was macerated for twenty-four hours. Then percolation was allowed to proceed slowly, adding more menstruum until the powder was exhausted.

Conclusions

1. Of the six different methods tried (digitonin-cholesterol, digitonin-alpha-naphthol, digitonin-beta-naphthol, digitonin-thiophenol, digitonin-terpineol, digitonin-bromo-naphthol) the best one was the digitonin-cholesterol. This method gave the highest results and showed that the addition compound formed is the least soluble, if at all.

2. From an economical standpoint the digitonin-alpha-naphthol or the digitonin-beta-naphthol method is the best. These precipitating agents cost least and can be easily separated from digitonin.

3. The addition compound, when extracted with hot xylene or benzene, can be separated into its component parts. The precipitating agents are soluble in the above-mentioned solvents while digitonin is not.

4. The quantitative estimation of digitonin showed that there is about 1.4% in the seeds, 31.1% in digitalin (Merck) and 81.1% in digitonin (Merck).

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FACTORS INFLUENCING THE PRODUCTION OF TERPINEOL FROM ALPHA-PINENE IN ACID SOLUTION

By Frederick G. Germuth

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THE AUTHOR has frequently observed the fact during the preparation of various organic compounds that slight differences existing in temperature during this period influence to a remarkable extent the yield and quality of the product sought. This observation appears to be particularly true in respect to the production of terpineol, $C_{10}H_{18}O$, by the action of benzenesulfonic acid in the presence of heat, on acetic acid solution of alpha-pinene.

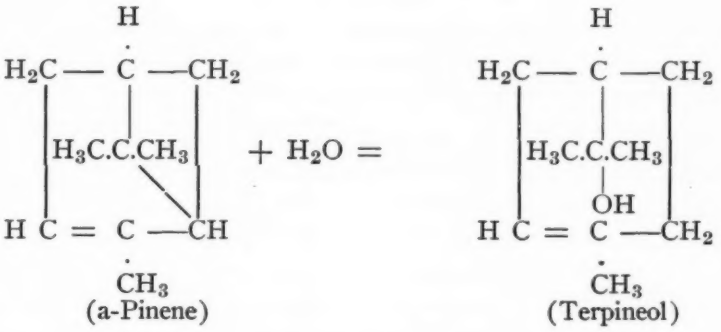
It was believed, also, that minute or larger portions of water present in the acetic acid solution of a-pinene would exert a retarding influence on the mechanism of the reaction taking place. Accordingly, steps were taken to prove or disprove the correctness of this view. The results of this undertaking are herewith presented.

The fact that numerical observations arrived at by the employment of chemical equations in calculating the amount of the products formed from molecular quantities of reacting compounds in reversible chemical reactions—in contra-distinction to those reactions of the irreversible type—do not conform to strictly stoichiometric standards in actual practice, is recognized by the chemist. Therefore, no attempt was made to compare the actual yield of the chemical compound produced with that quantity provided by theoretical consideration.

Gram-molecular combining quantities of the reacting substances were utilized; disregarding the law of mass action (Guldberg and Waage), an excess of either component was strictly avoided. Primarily, this was done to avoid the possibility of obtaining results that might prove misleading or confusing.

Hence, no effort was made to secure theoretical quantitative yields from the experimental portions of the compounds treated, the desideratum being comparative or relative figures obtained under dissimilar experimental working conditions.

The chemical transformation occurring when an acetic acid solution of a-pinene is heated with benzenesulfonic acid is graphically represented by:



Quality of Materials

As is evident, this reaction establishes the existence of the double-bond in a-pinene, and consists essentially in the acquisition of one molecule of water, and the consequent disappearance of the tetramethylene ring.

The a-pinene employed in the tests was obtained by the careful distillation of coniferous oleoresins. This was further purified by the process of redistillation, and found to possess a boiling point of 154.5° C., at a pressure of 756 millimeters of mercury. The a-pinene was sealed in a flask to prevent oxidation and subsequent resinification, until required for employment. The benzenesulfonic acid was of high quality, containing one and one-half molecules of water, few impurities, and none, it is believed, calculated to affect the reaction. The acetic acid was of glacial quality, chemically pure grade, consisting of crystals melting at 16.5° C. and possessing a boiling point of 118.4° C.

The Method

A portion consisting of 50 cubic centimeters of the glacial acetic acid was heated to room temperature and an amount of a-pinene calculated to react chemically with 2 grams of benzenesulfonic acid, dissolved in this. The latter was placed in this solution, and heated for one hour at 50° C. Similar quantities were treated under the same conditions excepting that of temperature, and the following results obtained:

Factors Influencing the Production of Terpineol From Alpha-Pinene in Acid Solution

TABLE NO. 1.

(Each sample containing 2 grams of benzenesulfonic acid in acetic acid solution of alpha-pinene, heated for one hour.)

	Temperature of Solution Degrees C.	*Percentage Conversion of Alpha-Pinene Into Terpineol.*
Solution No. 1	50°	55.82%
Solution No. 2	55°	58.45%
Solution No. 3	60°	62.09%
Solution No. 4	65°	65.71%
Solution No. 5	70°	69.88%
Solution No. 6	75°	71.02%
Solution No. 7	80°	72.42%
Solution No. 8	85°	73.01%
Solution No. 9	90°	73.42%
Solution No. 10	95°	73.61%

An attempt was next made to determine the effect of adding small amounts of distilled water to the acetic acid solution, in regard to the reaction. Employing the exact procedure as that utilized in obtaining the data given in Table No. 1, with the difference that the addition of water was resorted to, the figures presented in Table No. 2 record the results produced by an increase in water content:

	Temperature of Solution Degrees C.	*Percentage of H_2O Added.*	*Percentage Conversion of Alpha-Pinene Into Terpineol.*
Solution No. 1	50°	1.0%	53.96%
Solution No. 2	55°	1.5%	56.84%
Solution No. 3	60°	2.0%	60.71%
Solution No. 4	65°	2.5%	64.66%
Solution No. 5	70°	3.0%	68.14%
Solution No. 6	75°	3.5%	70.29%
Solution No. 7	80°	4.0%	70.86%
Solution No. 8	85°	4.5%	71.69%
Solution No. 9	90°	5.0%	72.76%
Solution No. 10	95°	5.5%	73.01%

The actual amount of a-pinene remaining, or that portion failing to combine chemically with the benzenesulfonic acid during treatment, was determined by taking advantage of the fact that it is an unsaturated hydrocarbon containing one double-bond. Dry hydrochloric acid gas was passed into the cooled solutions, and bornyl chloride, $C_{10}H_{16}HCl$, so called "artificial camphor," formed. The amount of the bornyl chloride produced was deducted from the original amount of a-pinene employed, *i. e.*, that proportion of a-pinene required to produce the specific amount of bornyl chloride obtained; and the conversion data calculated. As a further means of ascertaining the correctness of this method, the benzenesulfonic acid remaining in an uncombined state was determined by converting it into the sodium salt by the use of sodium carbonate, and then "salting out" by the addition of c. p. sodium chloride. Results secured in this manner checked very closely with those of the former method of determination.

Summary

It has been shown that differences in temperature affect very markedly the percentage yield of terpineol from benzenesulfonic acid and a-pinene in acetic acid solution. Addition of water, also, has a tendency to retard the production of this compound, more particularly at lower temperatures.

It is shown that when the amount of water added is increased from 1.0 per cent. to 5.5 per cent., with increase in temperature of the solutions, the effect upon the production of the substance sought is not proportional to the amount of water added; apparently, the differences existing in temperature compensate for the decided increase in the water content.

A temperature of about 95° C., employing a solution containing the least possible amount of water evidently insures the highest yield of terpineol from benzenesulfonic acid and alpha-pinene in acetic acid solution, when molecular quantities are employed.

DISINFECTANTS FROM LOW TEMPERATURE TAR.

By Frederick R. Greenbaum, D.Sc.
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IT WAS QUITE an obvious thought to try to use low temperature tar for disinfectants, thereby essentially increasing the field of application for this new kind of tar. Its high tar acid content and the high toxicity of the same seemed to suggest from the very beginning its use for disinfectants.

The disinfectants heretofore employed are combinations of ordinary high temperature tar oils with cheap soaps; for instance, rosin soap. "Creolin," is such a combination of rosin soap with cresols. A few drops of these disinfectants when put in water form white emulsions, which are used in households and farms on account of their high bactericidal and antiseptic properties. One customary commercial specification which is strictly adhered to on account of its salability, is the requirement that the emulsions must be perfectly white.

In the first series of experiments, combinations of low temperature tar distillate; low and high boiling low temperature tar phenols with rosin or castor oil soap were prepared. A drop of the so prepared disinfectants formed a perfect, white emulsion in water, thereby clearly demonstrating that low temperature tar is quite suitable for the preparation of disinfectants. Its disinfecting properties are far superior to those obtained from ordinary aromatic tar.

So the future of the low temperature tar and its application as disinfectants seemed rosy. Unfortunately, the emulsion also turned rosy after a few minutes of standing and assumed a distinct red color. This now offered another problem which caused a great deal of work and which has been solved only very recently.

As already mentioned above, one customary requirement for each disinfectant is that a white or yellowish white emulsion be formed. It would be extremely difficult to sell disinfectants from low temperature tar if the emulsions of these disinfectants assumed a red color, as the housewife as well as the farmer is accustomed to white emulsions. It was therefore of importance to find how the appearance of this red color could be avoided, or if possible, to establish the cause of the red color.

The first thought, that the red color which is formed a few minutes later, is a product of oxidation, was dropped and later again taken up.

It was believed at first that we were dealing here with an acid dye. As a matter of fact, if the emulsion was only faintly acidified, the pink color was transformed into a yellow color, only to reappear after the addition of alkalies.

Assuming, therefore, that an acid dye was being dealt with, 1 per cent., one-half per cent. and one-quarter per cent. sodium hydroxide were used. This actually extracted the dye, but at the same time, after two or three treatments with one-half per cent. sodium hydroxide, low temperature phenols were extracted to a considerable extent, which of course, was a great disadvantage. To avoid this, the writer employed 2 per cent., 3 per cent., 5 per cent. and 10 per cent. sodium carbonate solution. The oil was treated once or twice with sodium carbonate solution, allowed to settle, separated from the aqueous layer, washed with water and the residual water removed by heat. The oil thus obtained, when made into a disinfectant with rosin soap, gave a white emulsion which no longer turned pink when mixed with water. This apparently solved the problem.

The sodium carbonate solution which contained the dye was acidified and a black mass was obtained which was insoluble in water. It was soluble, however, in alcohol with red color and in sodium hydroxide with orange red color. The reactions of this dye pointed to the triphenylmenthane group, and as it was an acid dye, it was believed to be either rosolic acid or a derivative of rosolic acid. This rosolic acid is formed by oxidation of a mixture of phenol and cresol and it was quite plausible to assume that this dye could be formed during the low temperature carbonization of coal.

The so-developed method was recommended to the experimental factory. There a new batch of low temperature tar was distilled and the distillate washed twice with 2 per cent. sodium carbonate, in accordance with the method described above. The oil thus obtained was then transformed into a disinfectant and to our great surprise, in spite of the treatment with sodium carbonate which was supposed to have removed the dye, the emulsion turned red. So the problem came back into the research laboratory.

At this particular stage, in co-operation with Mr. S. Caplan, we went back to the oxidation theory previously mentioned. The reddish color of the emulsion appears only after a few minutes of

standing. While washing low temperature tar phenols with sodium carbonate solution in a separatory funnel, we observed that as long as the sodium carbonate solution was in the separatory funnel entirely excluded from air, it was completely colorless or had a very faint yellow color. As soon as the sodium carbonate was withdrawn from the separatory funnel, however, it assumed a strong reddish purple or dark purple color. This observation undoubtedly appeared to be an oxidation phenomenon. The rapid change in color from faint yellow to dark purple reminded us very much of pyrogallol, which in solution assumes rapidly a brown color due to the oxygen of the air. We therefore assumed that the substance which caused the red color of the emulsion of the disinfectant is a polyoxyphenol. As the polyoxyphenols are water soluble substances, it was quite natural to try to treat the low temperature oil two or three times with water.

This quite simple treatment, of two or three water washings, freed the oil entirely from all the dyeing ingredients. These water washings have, however, another disadvantage. Very often five to six washings are necessary and by this treatment a considerable amount of low temperature tar phenols go into solution, so that these water washings diminish considerably the content of low temperature tar phenols. Therefore another method was absolutely necessary. Distillation with milk of lime was tried but did not prove successful.

S. P. Burke and S. Caplan [1] continued to work on this problem and they succeeded in isolating and identifying the polyoxyphenol which is the cause of the red color of the emulsion of the disinfectants of low temperature tar oils. They found it to be 3-4 or 3-6 dimethylcatechol. Very recently they developed a method by which they are able to remove this dimethylcatechol by treatment with sodium borate without in any way changing the content of low temperature tar phenols, so that today low temperature tar can successfully be used for disinfectants which are superior in their phenol coefficients to the ordinary disinfectant from aromatic tar oils and which do no longer possess the objection of giving a red emulsion.

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PHARMACEUTICAL MANUFACTURING, FIFTY YEARS AGO AND NOW*

By F. W. Nitardy†

FIFTY YEARS AGO pharmaceutical manufacturing was still done, to a very large degree at least, in the drug store. I know that houses that are purveying manufactured articles to the retailer today were in existence at that time but they apparently were very small compared with what they now are and undoubtedly there were less of them. In fact, I remember that in my apprenticeship days we did a great deal of manufacturing in the retail store. It is hard for me to say whether that store was the exception to the general rule of that day or not; I am inclined to believe that it was a little old fashioned, reflecting the methods of an earlier day rather than those of its own day.

It is, however, within my memory that the Pharmacopœia has included assay processes, both chemical and physiological, for various preparations, and it is within my memory that the Food and Drugs Act has come into being, which gives real authority to the Pharmacopœia and the National Formulary as legal standards. While previously the Pharmacopœia was accepted by common consent, there was no law to enforce its mandates.

Obviously, it is very difficult for the pharmacist and altogether too expensive when considered from an economical standpoint to assay small lots of tinctures and similar preparations such as a pharmacist might make for his own use. It is perfectly logical therefore that the last twenty years have brought a considerable change in the attitude of a retailer toward making his own tinctures and similar preparations.

Furthermore, there has been a considerable advance in our scientific knowledge of drugs and therapeutic agents which has resulted in the decrease in use of a great many formerly more or less widely used products, the true action of which was more or less vague and unknown and the use of which probably was based largely on rather inaccurate empirical observations. The use of potent drugs whose action has been the subject of careful pharmacological study has, of

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course, increased and it is these drugs primarily that now are accurately tested and standardized.

Furthermore, there has been a considerable change in the retail store since I have known it, in that it has become more crowded and those engaged in the business seem to have less and less time to devote to manufacturing. Time has become much more valuable and those employed in a store apparently can make more money for the business by devoting their efforts to merchandising and filling prescriptions than by making up small batches of miscellaneous pharmaceuticals, which even if they were made in the store might get the owner into difficulty with the Food and Drug enforcement officials unless he were willing to go to the expense and trouble of assaying and standardizing them which, obviously, is either difficult or entirely impossible.

All of these things undoubtedly have contributed to building up the large and well equipped laboratories that we know today, with their splendid research and manufacturing facilities and which in fact contribute a great deal to the scientific advancement of pharmacy.

In the manufacturing field itself there undoubtedly have been changes brought about by the same agencies which have made the changes evident in the retail store.

During my own connection with the business I have seen a considerable advance in the employment of power and automatic machinery to replace, as much as possible, human effort.

The quality of medicinal products is ever being more closely guarded and constant research work is in progress in most of the larger laboratories on means and methods for more accurately testing and standardizing these products.

The War undoubtedly was one of the greatest factors in stimulating greater efficiency in the individual institutions, because it was at that time that the sharp advance in costs came about that made it absolutely necessary for manufacturers to study the question of doing their work with less labor, for the prices prevailing for finished products did not change materially and in many instances products of such laboratories can be purchased today for prices as low and sometimes even lower than they could before the War.

There undoubtedly also is a great trend toward standardization in all sorts of matters concerning the industry, such as standard sizes and shapes of containers, standard types of shipping cases, etc., so

as to eliminate the cost involved in unnecessary duplication of providing moulds and similar things, as well as eliminating unnecessary sizes or multiplicity of packings, etc., in which a given article formerly was available.

There also is a great tendency toward the elimination of multiplicity in manufactured items for which there is a limited demand. Practically every pharmaceutical house in the country has been deleting many of these products from its list. Undoubtedly the public, the retailer and the manufacturer will all benefit by the elimination from therapeutic use of a great many drugs of questionable merit which in the past have been encumbering the shelves of the retailer, the wholesaler and the manufacturer alike and which have served only to make prescribing by the physician more difficult. The sooner the materia medica is limited to a reasonable number of well understood and truly valuable drugs the sooner will the prescribing of these drugs again come into more general use and thereby the service rendered by all engaged in the pharmaceutical field become more valuable and in consequence more remunerative.

To sum up, I view the outstanding changes that have occurred as follows:

(1) The taking over of manufacturing activities largely by specialists, properly organized and equipped for such work.

(2) The great complication and great increase in cost involved in manufacturing, due to accurate assaying and standardization of finished products.

(3) Making the U. S. P. and N. F. legal standards of the United States.

(4) The effect of the food and drug laws, assay and standardization and concentration of manufacturing activities in well equipped laboratories with a scientific staff, resulting in the production of better and more reliable products generally (although it must be admitted that such products were obtainable prior to the food and drug acts even though they were by no means general).

(5) The development of labor saving machinery in manufacturing plants in order to meet conditions brought on by the War and to reduct costs..

(6) The gradual elimination from materia medica of many not widely used drugs of questionable merit, thereby concentrating interest in better known, more reliable and more active drugs.

STATE REGISTRATION REQUIREMENTS*

By H. C. Christensen

Secretary National Association of Boards of Pharmacy

THE FOLLOWING is a tabulation of state requirements to date (May 12, 1927), for registration, designating the dates on which the high school and college of pharmacy graduation requirements went into effect. These tabulations with the addenda which follows are, I believe, self-explanatory.

Relative to the states having reciprocity: New Jersey has recently been added to the list so that we now have forty-five states and the District of Columbia.

The new California law also includes a provision for reciprocity, but inasmuch as the privilege has been restricted to college graduates, it is doubtful whether that state can qualify for membership in the N. A. B. P. thereby securing reciprocal relations with the other member states. A state in order to hold membership in the N. A. B. P. and through its membership participate in reciprocity, must abide by the constitution and by-laws of the Association and be willing to adopt the general rules and regulations governing reciprocity. The chief of these requirements is that a state must be willing to grant reciprocal registration to an applicant from another state, provided such applicant had the legal qualifications at the time of examination and registration in the state from which he applies which would, at the time of such examination and registration, have entitled him to take examination and become registered in the state to which he applies for reciprocal registration. That is the point which California seems to have overlooked. There is no provision in the new law of that state for granting reciprocal registration to a non-graduate pharmacist from another state who registered in such state prior to the time the California college graduation requirement becomes effective, and because of the law not doing so may result in nullifying the proposed reciprocity for graduates.

*Presented at the 1927 meeting of the Pennsylvania Pharmaceutical Association.

State Registration Requirements

State	*High School Graduation*	*College Graduation*	*Experience and Other Requirements Present*
Ala.	1/1/27	1/1/27	4 yrs. exp. 2 yrs. credit for college graduation.
Ariz.			4 yrs. exp. Credit for actual college time. 2 yrs. high school.
Ark.	1/1/25	1/1/25	4 yrs. exp. 2 yrs. credit for college graduation.
Calif.	1/1/28	1/1/28	5 yrs. exp. 2 yrs. credit for college graduation. Grammar school.
Colo.			4 yrs. exp. 2 yrs. credit for college graduation. Grammar school.
Conn.	1/1/23	1/1/25	4 yrs. exp. 2 yrs. credit for college graduation.
Dela.	3/30/27	3/30/27	4 yrs. exp. 2 yrs. credit for college graduation.
D. C.	3/4/28	3/4/28	4 yrs. exp. 1 yr. credit for college graduation.
Fla.	6/1/28	6/1/28	4 yrs. exp. Credit for actual college time if graduate. 2 yrs. H. S.
Ga.	7/1/27	7/1/27	3 yrs. exp. or college graduation without experience. 2 yrs. H. S.
Ida.	5/1/25	5/1/25	4 yrs. exp. 2 yrs. credit for college graduation. Apprentices prior to 5/1/25 exempted from college graduation and H. S. until 5/1/30.
Ill.	1/1/20	7/1/17	4 yrs. exp. Credit for actual college time not to exceed 2 yrs.
Ind.	7/1/23	1/1/20	4 yrs. exp. Credit for actual college time.
Ia.	7/1/25	7/1/17	4 yrs. exp. (2 yrs. exp. and 2 yrs. college) or (1 yr. exp. and 3 yrs. college).
Kans.	5/25/21		4 yrs. exp. or (2 yrs. exp. and 2 yrs. college) or (4 yrs. college).

Credit for actual college time. 4 yrs. exp. Credit not to exceed 30 months of attendance at college.

2 yrs. college attendance.

State	*High School Graduation*	*College Graduation*	*Experience and Other Requirements Present*
Ky.	1/1/26	7/1/24	4 yrs. exp. Credit for actual college time not to exceed 2 yrs.
La.	1/1/27	1/1/27	4 yrs. exp. Credit for actual college time.
Me.	7/1/27		4 yrs. exp. or 1 yr. exp. and college graduation. 2 yrs. H. S.
Md.	6/1/20	6/1/20	4 yrs. exp. 2 yrs. credit for actual college time.
Mass.			4 yrs. exp. Credit for actual college time. No provision for preliminary education.
Mich.	1/1/24	1/1/29	4 yrs. exp. 1/1/23—3 yrs. credits for 3 yrs. college.
	2 yrs. college attendance.		
Minn.	1/1/20	4/25/19	4 yrs. exp. (2 yrs. exp. and 2 yrs. college) or (1 yr. exp. and 3 yrs. college).
	2 yrs. college attendance.		
Miss.	1/1/21	1/1/21	No experience requirement. Regis. without state board examination granted on diploma of University of Mississippi School of Pharmacy.
Mo.	1/1/23		4 yrs. exp. Credit for actual college time not to exceed 2 yrs.
Mont.	1/1/26	1/1/26	4 yrs. exp. Credit for actual college time up to three years.
Nebr.	7/1/20		3 yrs. exp. or (4 yrs. college) or (2 yrs. exp. and 2 yrs. college).
Nev.	1/1/14		5 yrs. exp. Credit for actual college time.
N. H.	1/1/27		4 yrs. exp. 2 yrs. credit for college graduation.
N. J.	1/1/24	2/1/20	4 yrs. exp. 7 mos. credit for each college term up to 2 yrs.
N. M.			3 yrs. exp. Credit for actual time in college. 1 yr. H. S.
N. Y.	1/1/25	1/1/04	4 yrs. exp. Credit for actual college time.

State	*High School Graduation*	*College Graduation*	*Experience and Other Requirements Present*
N. C.	1/1/22	1/1/22	4 yrs. exp. Credit for actual college time.
N. D.	1/1/23 After 7/1/27—3 and 4 yr. graduates required to have only 1 yr. experience.	1/1/15	4 yrs. exp. 2 yrs. credit for college graduation.
Ohio	1/1/20	8/26/15	4 yrs. exp. 2 yrs. credit for college graduation.
Okla.	7/16/21	1/1/23	4 yrs. exp. Credit for actual college time not to exceed 2 yrs.
Ore.	1/1/18	(7/1/22 2 yrs.) (7/1/25 Grad.)	4 yrs. exp. 2 yrs. credit for college graduation.
Pa.	6/1/25	1/1/06	3 yrs. exp. Credit for 1 yr. for college if employed while attending.
R. I.	Grad.	Grad.	3 yrs. exp.
S. C.	1/1/23	7/1/18	4 yrs. exp. Credit for actual college time.
S. D.	1/1/27		3 yrs. exp. or college graduation and 1 yr. experience.
Tenn.	1/1/20		4 yrs. exp. 2 yrs. credit for college graduation.
Texas	1/1/26		4 yrs. exp. 2 yrs. credit for college graduation.
Utah	7/1/25	7/1/27	4 yrs. exp. Credit for actual college time not to exceed two years. Assistants registered as such prior to July 1, 1927, exempted from college graduation until Jan. 1, 1928.
Vt.			3 yrs. exp. Credit for actual college time. Grammar School.
Va.	4/1/22	4/1/22	College graduation. No. exp.
Wash.	7/1/14	7/1/14	(2 yrs. exp. and 2 yrs. college) or (1 yr. exp. and 3 yrs. college) or (4 yrs. college and no exp.).

State	*High School Graduation*	*College Graduation*	*Experience and Other Requirements Present*
W. Va.	1/1/23	1/1/23	4 yrs. exp. credit for actual college time.
Wis.	1/1/26		5 yrs. exp. or 2 yrs. exp. and college graduation.
Wyo.	1/1/25		3 yrs. exp. 1 yr. credit for college graduation.

Forty-four (44) states now have high school graduation in force or to become in force either by law or ruling of Board or by virtue of requiring graduation from recognized schools or colleges of pharmacy which require high school graduation for entrance to courses.

Thirty-three (33) states now have in force or to become in force provisions for college of pharmacy training,—all excepting three, Iowa, Minnesota and Michigan, require graduation. The three states named provide for two years of attendance at a college of pharmacy but not graduation. Under the present two-year college course, this usually meant graduation, but not so under the present three-year course.

California, Delaware and District of Columbia enacted legislation this year requiring college graduation. In Wisconsin a law requiring graduation is still pending and prospects for enactment are reported favorable. In Colorado, South Dakota and Texas college prerequisite legislation was defeated, chiefly, it is reported, because the enactment of complete new pharmacy laws was attempted, some of the provisions of which engendered opposition strong enough to defeat the proposed laws in each of these states.

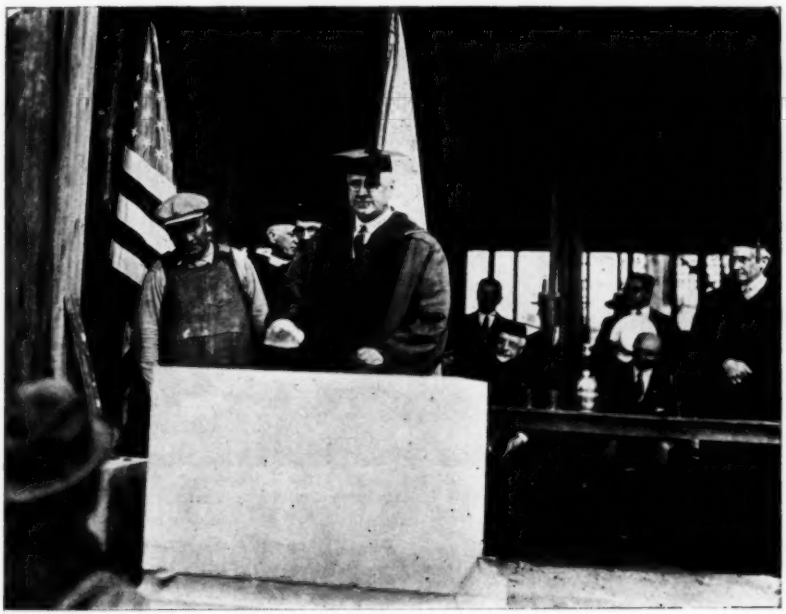
Texas reports that at a special session of the legislature of that state an attempt will now be made to amend the present law so as to require college graduation, instead of again trying to pass a new law.

THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE.

LAYING THE CORNER STONE OF THE NEW BUILDINGS

THE ONE HUNDRED AND FIFTH ANNUAL COMMENCEMENT EXERCISES

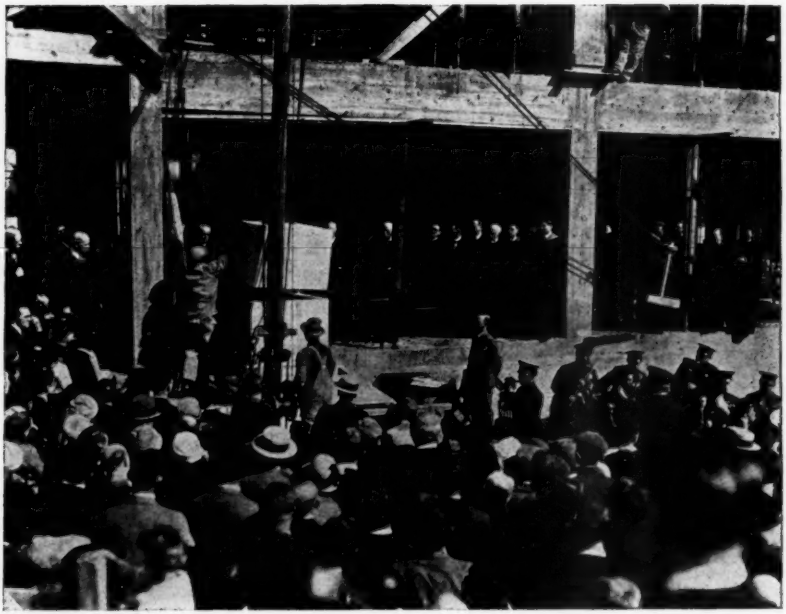
ON Tuesday, June 7th, the Philadelphia College of Pharmacy and Science laid the cornerstone of its new buildings at Forty-third Street and Kingsessing Avenue, West Philadelphia. The occasion was attended by a vast throng of alumni and friends of the Institution. Music was furnished by the Municipal Band. The College is the oldest pharmaceutical school in the United States, its



President Krusen Laying the Cornerstone

establishment dating from 1821. Work on the new buildings will go forward rapidly to enable the College to open there for its January term.

The buildings, designed by Norman Hulme, consist of a three-story main structure of reinforced concrete, and two flanking wings, with an exterior of Colonial brick and limestone trim. Special attention has been given to laboratories, and ample provision made for special research work. The library has shelf capacity for 50,000 volumes. When completed the building will represent the latest developments in arrangement of class rooms, laboratories, etc., for institutional scientific and technical instruction.



Laying the Cornerstone of the New Philadelphia College of Pharmacy and Science

At the cornerstone laying the program was initiated by Dr. Wilmer C. Krusen, President of the College, officiating as Presiding Officer, with Dr. Charles H. LaWall, Dean of Pharmacy, in charge as Master of Ceremonies. The Invocation was given by Rev. Louis C. Washburn, Rector of Christ Church.

Among those participating in the exercises were:

Dr. Theodore J. Bradey, of Boston, Dean of the Massachusetts College of Pharmacy and President of the American Pharmaceutical Association, who after a brief address, presented the trowel;

Mayor W. Freeland Kendrick, presented the gavel made from one of the original beams of Independence Hall;

Joseph W. England, President of the Pennsylvania State Pharmacy Association, had charge of the copper box which was deposited in the stone. In this sealed box had been placed messages for the future, written by a score or more prominent figures in pharmacy;

Professor Frank X. Moerk, President of the Alumni Association and Hon. George A. Welsh, Member of Congress from the West Philadelphia District, made brief addresses;

The oration was delivered by Alba B. Johnson, President of the Jefferson Medical College. Dr. Johnson gloried in the fine reputation of the old College and outlined its great possibilities for future humanitarian service.

The progress made since breaking ground for the buildings has been nothing short of marvellous and it is hoped that the work of the College will be transferred to the new location about the first of January, 1928.

The One Hundred and Fifth Annual Commencement of the Philadelphia College of Pharmacy and Science

The one hundred and fifth annual commencement of the Philadelphia College of Pharmacy and Science, was held in the Aldine Theatre at 10.30 o'clock on Wednesday morning, June 8th, in the presence of a large and interested audience.

The Rt. Rev. Thomas J. Garland, D.D., Bishop of Pennsylvania, pronounced the Invocation. The graduates were presented to Dr. Krusen, President of the College, by Dr. J. W. Sturmer, Dean of Science, and Dr. Charles H. LaWall, Dean of Pharmacy.

Degrees were conferred on forty-nine students, representing the group graduating during the first year in which the newly-established three-year course operated. The Master in Pharmacy (*Honoris Causa*) degree was conferred upon three prominent pharmacists.

One of the recipients was Sir William S. Glyn-Jones, of England, at present located in Montreal, Canada, in charge of certain

work instituted by the Canadian Pharmaceutical Association. Sir Glyn-Jones has spent his entire life in pharmaceutical educational work, successfully introducing in Great Britain the Proprietary Articles Trades Association, which Society he served as secretary for many years until invited to institute a similar work in Canada. He has spent considerable time in the United States in study and investigation.

Another recipient of the degree was Dr. Robert J. Ruth, of Philadelphia, who two years ago instituted National Pharmacy Week in the United States. This work has been so successful in educating the public in the work of the pharmacist as an important factor in safeguarding the health of the community, that last year Pharmacy Week was also established in Australia, New Zealand and Canada.

The third recipient of the degree was Daniel H. Hills, of Spring Lake, New Jersey, who has been for ten years a member of the New Jersey Board of Pharmacy and was elected to the presidency of the Board last year. For nearly forty years Mr. Hills has devoted himself to the advancement of his profession and the maintenance of its high standards in practice.

A most inspiring address* was delivered by Dr. Edgar Fahs Smith, of the University of Pennsylvania.

Degrees in courses were conferred upon the following:

Master of Science (M.Sc.) in course

McDonnell, Joseph Francis, Jr. Mellanoff, Isadore Sidney
Schaeffer, Harry Joseph

Bachelor of Science in Pharmacy (B.Sc.)

Crawford, Ruliff E. Lee, George Arthur
Kartyn, Harry Yaffey, Benjamin Edward

Bachelor of Science in Chemistry (B.Sc.)

Deuble, John Lewis Rees, Edward William
Pines, Charles C. Strock, Lester W.

Bachelor of Science in Bacteriology (B.Sc.)

Loehle, Joseph N. McCoy, Agnes E.
Sayenko, Anastasia

*This address appears elsewhere in the Journal.

Pharmaceutical Chemist (Ph.C.)

Acton, Morris G., Jr.
Brockman, Frank G.
Panton, James H.
Tong, Young
Wilkins, Elwood Smith, Jr.

Bachelor in Pharmacy (Phar.B.)

Busigo, Juan Gaulberto
Farber, Maxwell M.
Kraemer, Edward
Margolis, Aaron H.
Perog, Walter
Shiley, Norman J.
Smith, Andrew J.

Graduate in Pharmacy (Ph.G.)

Ackerman, H. W.
Blaustein, M. J.
Bohr, John E.
Braude, R. L.
Brown, C. A.
Coda, T. P.
Coleburg, C. L.
Dezenhall, S.
Feicht, P. A.
Fino, P. J.
Granahan, J. V.
Gwinner, Anna
Hoch, Leroy
Hoffman, C. J.
Lansberry, Lois E.
Maffucci, H. G.
Morinelli, Josephine
Nice, John
Salaman, L.
Sharp, Warren
Simpson, G. J.
Yanoff, Fannie
Young, Ralph

STUDENTS WHO HAVE COMPLETED SPECIAL COURSES AND QUALIFIED FOR CERTIFICATES

(This does not include students who completed courses in these subjects for credits for a degree)

In Bacteriology

Bernstein, Max
Brown, Nathan M.
Donahue, Mary A.

In Clinical Chemistry

Brown, Ruth E.
Brown, Nathan M.
Donahue, Mary A.
Haussmann, Herman William
Trivelli, Philip F.
Stoneback, William J.

PRIZES

The Bacteriology prize, $25, offered by the H. K. Mulford Company, to the candidate for graduation making the highest general average, and the highest grade on a special examination, in Bacteriology and Serum Therapy, was awarded to

J. F. McDONNELL, JR.

With Honorable Mention to

Juan G. Busigo
J. F. Loehle
Elsie A. McCoy
A. Margolis
C. C. Pines

The Advanced Pharmacy Prize, ten dollars' worth of books, offered by Professor Charles H. LaWall, for the highest grades in Advanced Pharmacy, to third and fourth year students, awarded to

HARRY KARTYN

PRIZES AWARDED BY THE ALUMNI ASSOCIATION

The Alumni Silver Medal for the highest general average in all branches in the second year of the Ph. G. Course is awarded to

ALBERT HOLTZ

The Alumni Bronze Medal for the highest general average in all branches in the first year of the Ph. G. course was awarded to

LINWOOD FRANKLIN TICE

ABSTRACTED AND REPRINTED ARTICLES

OCCURRENCE AND HABITS OF OUR POISONOUS SNAKES*

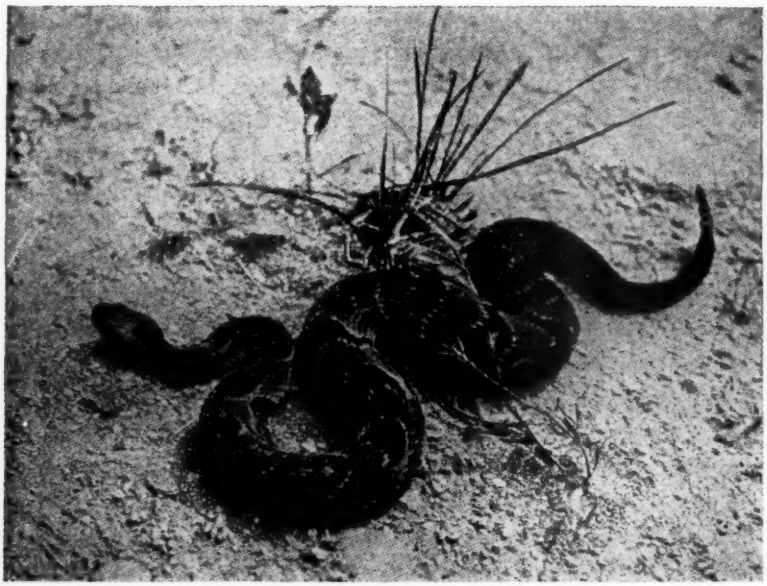
By Raymond L. Ditmars

PRACTICALLY every portion of the United States is inhabited by poisonous serpents—although we might accord to a few states in the northeastern corner of this far-flung area the reputation of being nearly or quite free of them. These are the states of Maine, New Hampshire and Vermont. We cannot altogether clear Vermont, as there are occasional reports of rattlers in the southerly portion. The northerly states to the westward are liberally inhabited by rattlesnakes, and these reptiles extend their habitat well into Canada. This condition extends westward to the Pacific Coast. Our southeastern states, warmed by their contact with the Gulf Stream, with thick tangles of river swamps and coastal areas conducive to the existence of reptile life, harbor large numbers of poisonous serpents. Texas, Arizona and New Mexico are very liberally supplied with rattlers. The Pacific states have large numbers of rattlesnakes, while the interior states show "spotty" occurrence, abundant in some areas, moderately so in others—but let us come back East again. The writer doubts if there are any portions of the United States more abundantly supplied with venomous snakes than some areas of Massachusetts, Connecticut, New York, New Jersey and Pennsylvania.

There is one curious thing about the distribution of some species of our poisonous snakes. They are so thoroughly "in our midst." The writer bears in mind important summering towns of our eastern states where venomous reptiles extend their domains to within a few minutes' motor ride of Main Street. It is not necessary to go far into the wilds to find several of the venomous species. One may stand on fashionable Riverside Drive in New York City, and without a field

*Reprinted from *Bulletin of the Antivenin Institute of America.*

glass look northward and across the Hudson to rocky areas inhabited by copperhead snakes. From records at hand we believe that copperhead snakes still exist within the actual northern boundaries of New York City. During the past two years we received more than three dozen large copperheads captured within the city limits of a thriving community about twenty minutes' motor run from the boundaries of the Bronx.



A Typical Banded Rattlesnake (Crotalus horridus)

A detailed description of the distribution of our poisonous reptiles is of practical interest. There are more than a dozen distinct species or "kinds" of rattlesnakes, varying in size from one that is smaller than the average garter snake to the huge and formidable Diamond-back, which attains a length of nearly nine feet, a circumference of about twelve inches and weighs up to fifteen pounds. Throughout the whole northeastern portion of the United States there is but a single species—the Banded or Timber Rattlesnake. In

western New York a small rattler—the Massasauga—is occasionally found and becomes rather common in the eastern central states. The timber rattlesnake gives way on the eastern plains to a species of wide distribution—the Prairie Rattlesnake—which again gives way, in approaching the Pacific region, to the Pacific Rattlesnake. Going south, in the East, we find another rattler from about the central portion of North Carolina. This is the diminutive Pygmy Rattlesnake, often called the "Ground" Rattler. The latter term is misleading and inappropriate, as all the rattlers are strictly terrestrial. A bit farther south is the range of the big southern Diamond-back, which attains the greatest length of any rattlesnake in the United States. The Mississippi Valley forms the western boundary of this deadly brute, its place being taken in Texas, thence westward to eastern California, by the big Diamond-back of the arid regions—a close second in size, attaining a length of seven feet or more. Going westward into the habitat of this species, we enter the headquarters of the rattlesnakes of the southwest. At least five species of rattlesnakes are found in Texas, but the southwestern states may "boast" ten or more distinct kinds, among these being the almost white Mitchell's Rattlesnake, the Red Rattler and the curious Sidewinder. The last never leaves the deserts, and living on soft and yielding sand, has become highly specialized in locomotion, throwing lateral loops of the body, instead of crawling, and thus moving off rapidly in what appears an oblique direction to that in which its head is pointing. With the exception of two species, the rattlers feed upon warm-blooded animals—mammals and birds. The two species of *Sistrurus*—the Pygmy Rattlesnake and the little Massasauga—feed largely upon frogs, but also upon warm-blooded prey.

All the species of rattlesnakes, large and small, may be immediately distinguished by the unique caudal appendage—the rattle. The amateur naturalist, prospector or farmer is not particular as to the exact species; what he is desirous of knowing is whether a snake is dangerous. The possession of a rattle shows this to be invariably the case.

In the distribution of our poisonous snakes, we have yet to consider the two species of moccasins—the Water Moccasin and the Cop-

perhead Snake (Highland Moccasin, Pilot Snake, Chunkhead, etc.). These belong, as do the rattlers, to the family of Pit Vipers, having a deep pit on each side of the head between the eye and the nostril. Here is a strong character for identification. The Water Moccasin is dull olive, with wide transverse darker bands, and is common in the swamps and sluggish waterways of South Carolina, Georgia, Florida, Alabama and Louisiana—also portions of adjoining states. The Copperhead Snake is pale brown, and crossing this ground color are rich reddish brown bands, usually narrow on the top and very wide on the sides, appearing when examined from above like the outlines of an hour-glass. Texas specimens are rather characteristic in having fewer and much wider bands. The distribution of the copperhead is quite extensive. The species ranges from southern Massachusetts to northern Florida, westward to Oklahoma in the South, to Illinois in the northerly portion of its distribution. It will thus be understood that over the greater portion of the West the only type of poisonous serpent is the rattler.

In our southeastern states, thence along the United States-Mexican boundary, there are two small poisonous serpents of brilliant coloration known as Coral Snakes. They are New World allies of the members of the Cobra family. (Both species of the Coral Snakes (*Micrurus*) inhabit the southern part of this country. The common Coral Snake or Harlequin Snake occurs from southern North Carolina to Florida and westward to Texas. It is most abundant in Georgia, Florida, Alabama and Louisiana. The Sonoran Coral Snake is restricted to Arizona, New Mexico and northern Mexico. Both species are vividly ringed with scarlet, yellow and black—the red and black rings the broadest. Their pattern is wonderfully striking, imparting a really artificial aspect, like a gaudy necklace.

Described in detail, the pattern of the Coral Snakes may be given as broad, alternating rings of red and black, the latter bordered with very narrow rings of yellow. And here we encounter a difficulty: for several harmless snakes "mimic" these species in displaying exactly the same colors, arranged in ring-like fashion. Yet there is one unvarying difference that will always distinguish the dangerous reptile

from their innocuous "imitators": the yellow rings of the poisonous snakes always border the black rings, while among the non-venomous snakes there are pairs of black rings bordering a yellow one.

The Coral Snakes are rather secretive in habits and are often plowed up in the fields. They feed mostly upon small species of innocuous serpents.

Near and frequent contact with humans appears to have influenced the habits of our eastern reptiles. They usually keep close to sheltering holes or crevices, and when disturbed seek to escape as quickly as possible. Or they may try other tactics and remain quite motionless, with the idea of the intruder passing them by unnoticed. They are not nearly so vicious or apt to strike as the poisonous reptiles of the southerly latitudes. Accidentally stepped on or touched by the hand of the careless climber, they will instantly bite, as they are extremely nervous. They are to be seriously reckoned as a hazard in these days of hiking, camping and auto picnicking, as the great majority of our growing legions of outdoor enthusiasts are quite devoid of woodcraft. The fields and woods are filled with novices from the cities, the women wearing silk stockings and knickers, the men shod in low shoes and the children generally running wild. It is quite astonishing that so few accidents are reported in the north, and the condition must in a measure be attributed to the mild temper of the northerly snakes. There is no doubt that many a picnicker has had his unprotected ankles within striking distance of a copperhead, but has blissfully rambled onward.

Neighboring farms, the prowling of domestic animals, near and frequent contact with man, would appear to explain the points outlined and other interesting observations. Motor highways seem to have influenced the prowling of reptiles. These seem to form barriers to their crossing. Whether or not it is the cement or asphaltum surface or the odor from dropping oil, coupled with the slow disintegration from porous surfaces of exhaust gases, is hard to say, but certain it is that few poisonous serpents are seen these days crossing a motor highway. A few years back they were frequently killed on the roads of dirt or rough macadam. These conditions do not result

from any growing scarcity of the reptiles. They are just as abundant as they ever were over wide areas split by motor roads. They have stopped crossing the roads, and the rural police of several states have told the writer they have frequently noted snakes crawling through culverts and think that they prowl along the sides of the roads under cover—seeking a way to go under the new barrier.

The serpents of our northern and central states, except the open or prairier portions, have other habits differing from those of the South, as they return each year to areas of shattered rock in order to hibernate. They congregate at these specific places or "dens" in considerable numbers and probably come distances of several miles—guided by that strange instinct that prompts the fall migration of birds. As they scatter from the "dens" in the spring they usually follow the outcrops of the ledges, these offering numerous crevices for escape and shelter, and forming the abode of small rodents, upon which they largely feed. It is this habit of keeping in mind the friendly crevice that prompts them to escape, when frightened, rather to strike at the intruder.

Conditions are different in the South and over a considerable portion of the mild Pacific region, Rattlesnakes wander over fairly open country or wide areas of sand. They carry no assurance of a nearby sheltering crevice and when surprised will instantly flash into a fight for life. There is an immediate buzz of the rattle and a stab of poison-conducting fangs if the intruder is within striking distance —the serpent being able to strike slightly over one-half the length of its body. The intent of the snake is to drive an envenomed blow and to escape during the time the enemy is thrown into confusion by the realization of his receiving a poisoned bite. If there is no sheltering vegetation or other means of hiding near by, the rattler may remain coiled and defiant, sounding its warning and ready to repeat the blow. A snake may strike from a clump of greasewood or sage, or from under the broad, low leaves of dwarf palmetto. Such spots should be avoided unless one is shod with heavy canvas or leather leggings. A pair of leather puttees, reaching from the knees over the shoe-tops, offer ninety per cent. protection.

MEDICAL AND PHARMACEUTICAL NOTES

TEA IN TREATMENT OF BURNS—Tannic acid has been used in the treatment of burns rather extensively in Shen's clinic, and its efficacy has been amply demonstrated. It occurred to him, however, that as the principal active ingredient of tea is tannic acid, it might be possible also to use strong infusions of tea for the treatment of burns. It further occurred to him that as tea is the beverage in China, as well as in the other Oriental countries, a common therapeutic measure for burns might be developed which can be readily used in any household. The fifteen minute, 8 per cent., infusion of average green or red (black) tea is considered as most suitable for the treatment of burns. The infusion can be sterilized by boiling for three minutes. Good results are reported.—*China Med. Jour.* **41**: 150 (Feb.) 1927, through *Jour. A. M. A.*

COD LIVER OIL CONCENTRATE—A cholesterol-free concentrate, prepared by the method described by Kramer *et al.*, was found to be as potent as cod liver oil itself in amounts equivalent to the original oil. The concentrate, when injected subcutaneously in an ether solution, cured experimental rickets in rats. The same concentrate is inactive when injected subcutaneously with palmitin as the solvent.—*Jour. A. M. A.*, July 11, 1927.

DYESTUFFS IN GLYCERIN EFFICIENT ANTISEPTICS—Pleth asserts that glycerin is a very efficient antiseptic, yet not toxic to the leukocytes in strength below 41 per cent. Glycerin dyestuff suspensions do not cause irritation in the most painful wounds. Suspensions of dyestuffs in 25 per cent. propyl alcohol have proved to be excellent skin disinfectants. The best bactericidal results can be had by applying the solutions hot. Not only are the dyestuff solutions more toxic for gram-positive bacteria when applied hot than when applied cold,

but also when applied hot they become bacteriostatic for certain gram-negative organisms on which, when applied cold, they are quite without effect. The healing time of infected founds is materially reduced by this method.—*Amer. Jour. of Surg.* **2**: 239 (March) 1927, through *Jour. A. M. A.*

Effect of Antiseptics on Nasal Flora—The observations made by Bull and Bailey seem to eliminate the possibility of freeing the upper respiratory passages of rabbits of pathogenic organisms by treatment with antiseptic solutions. Solutions of mercurochrome, zinc sulphate, mild silver protein (argyrol), phenol (carbolic acid), dichloramine, acriflavine, crystal violet and brilliant green, allowed to run into the nostrils of rabbits, were devoid of beneficial influences, either in affecting the nasal discharges associated with snuffles or in removing pathogenic organisms. Mercurochrome seemed to cause *Bacillus bronchisepticus* to disappear from the nasal secretions. Some of the other drugs, particularly dichloramine, crystal violet and brilliant green, caused a reduction in the number of the less pathogenic organisms, but this was accompanied by an increase of the more pathogenic ones. Mercurochrome, zinc sulphate, mild silver protein and phenol apparently did not cause injury to the mucous membranes. Acriflavine seemed to be slightly irritant. Dichloramine, crystal violet and brilliant green were definitely injurious, causing profuse nasal discharges. Pneumonia frequently developed following the use of crystal violet, and rather regularly after the use of brilliant green.—*American Journal of Hygiene*, **7**: 105-109 (March) 1927, through *Jour. A. M. A.*

"Posting" Mummies—It was the first duty of every pious Egyptian to provide, while living, for the careful mummification and worthy burial of his body, in order that his existence, after death, in the world beyond might be happy and more beautiful.

For the medical investigator, there is interest in examination of mummies for traces of pathologic changes of any kind, in order to gain an insight into the condition of health among the ancient Egyp-

tians, who are known to have had a comparatively highly developed art of healing.

Marked anatomic malformations and changes were, of course, the easiest thing to discover. For example, on the mummy of Pharaoh Siptah, of the nineteenth dynasty, a typical club foot was found. Numerous bone fractures were discovered, especially of the forearm; on the mummies in question there were, in some cases, artfully contrived splints. Bladder stones were found in mummies dating back to periods preceding the first dynasty. Kidney stones were found only as far back as 3200 B. C. In a mummy of the fifteenth dynasty a case of tuberculosis of the spine was established. Cancerous ulcers were not found until the Byzantine period was reached. Gouty changes were discovered in the mummy of an aged man. The feet especially were involved, and, more particularly, the great toes. The knee joints and the patellar ligaments were markedly penetrated with a white substance. White, chalklike deposits, which on chemical examination gave the typical reactions to uric acid, were found in the wrist and arm joints.

The observations made on the teeth of mummies are very interesting. In the oldest periods bad teeth were rare and in the poor population bad teeth were lacking. They were comparatively frequent, however, in the bodies of the kings. The 500 bodies of Egyptians of the uppermost class, which were excavated near Gizeh, presented tartar formation and dental caries to an extent almost equal to that of the modern European.

In the mummy of an Ammon priestess of the twenty-first dynasty an extensive pelvic abscess was found, and in the face of the mummy of Rameses V a peculiar skin change was noted which resembled smallpox scars.

The most important result for the science of medicine was the fact that changes indicative of syphilis could not be found on the mummies, which constitutes further evidence for the belief that syphilis was unknown to the ancient world. The mummies furnish likewise valuable material for the study of leprosy. The only case of leprosy that could be found in a mummy dated from the late Christian epoch, which strengthens the assumption that the leprosy of the Jews

of Biblical times, *"zaraath,"* has nothing to do with genuine leprosy—that the leprosy of ancient times was a different disease the exact nature of which can be explained only by further researches in the field of historical medicine.—*Jour. A. M. A.,* June 11, 1927.

Destruction of Germs By Ammonia and Chlorine.—Through the results of the bacteriological and chemical examination of water in a swimming bath, after treatment with chlorine and ammonia, are described. The gases, which are used in the ratio of two parts of chlorine to 1 part of ammonia by weight, probably owe their bactericidal effect to chloramine. Compared with the use of chlorine alone, the method has the advantage that no odor of chlorine is perceptible, the water remains clearer, and a careful regulation of the amount to be added is not required.—*Chemistry & Industry,* May, 1927, p. 382-B.

A New Slant on the Smoke Nuisance.—Control of the smoke nuisance must depend upon the effect of smoke-laden air on health, if success is to be achieved, according to Dr. Charles White, pathologist of the United States Health Service, who points out in *American City,* that smoke prevention will be more readily secured if it can be shown that smoke-laden atmosphere has a harmful effect on the human system. The chief arguments heretofore have been for comfort and cleanliness. Data collected by him show that the city of Pittsburgh has a low tuberculosis death rate but a high pneumonia death rate, an analysis by wards showing that the higher rates occur where the smoke-laden air is denser. The number of physicians specializing in respiratory diseases is higher per capita in Pittsburgh than in Baltimore, showing a greater demand for this type in the smoke areas. The evidence indicates that smoke must be controlled from the viewpoint of its effects upon public health.—*Scientific American,* July, 1927, p. 74.

Unseen Life of Soil Plays Important Role.—Unseen and unknown to almost everyone, invisible because of their microscopically small size and always hidden n subterranean darkness, there is a whole swarming world of life under our feet. Its members are

often weird in form, sometimes beneficent, sometimes harmful in their acts, but never for a moment, day or night, without their effect on the giant world of plants and animals and men that live forgetfully above them.

This world of the soil microbiota, forgotten or ignored by all save a relative handful of scientists scattered over the earth, was outlined before the First International Congress of Soil Science here by Sir John Russell, director of the oldest and greatest agricultural experiment station in the world, at Rothamstead, England.

The effects wrought by soil bactera, fungi, protozoa and other forms of life are manfold. Lowly plants called algae capture carbon dioxide from the air, build it into their bodies, and eventually, when they die, release their organic substances as humus for the enrichment of the soil. Many kinds of soil bacteria, both free-living and associated with other plants, are able to capture the otherwise inert and useless nitrogen gas from the air, which is eventually turned by the higher plants into meat-making proteids.

Bacteria break down dead plant and animal bodies, returning them to the dust from which they came; if it were not for this activity the earth's surface would soon be cumbered with carcasses, with all the material basis of life locked up in them beyond recovery. This process is not a smple one, carried on by only one class of bacteria.

One gang of these microscopic wreckers goes to work, carries the process as far as its nature permits, and then quits. Another takes its place, forwards the work another stage, and in its turn passes it on to still other groups. At last the complex substances of the dead body are again the simple compounds that plants can use, and the upbuilding process begins once more.

Tearing down is as important a process in the cycle as setting up; for there are only just so many bricks for life to build with, and they must be used over and over. These lowly creatures of the soil, which may be our own unrecognized evolutionary ancestors, do the cosmos a service by plucking down our abandoned dwellings so that our descendants may make houses for themselves.—*Science Service.*

Breath of Bacteria Becomes Plant Food.—The breath of bacteria, the carbon dioxide discarded by them as a by-product of their life-processes, comes to man's table as his daily bread. We live on the exhalations of billions of tiny beings which we never see.

This, in brief paraphrase, is the revolutionary doctrine laid before the First International Congress of Soil Science, by Dr. Julius Stoklasa, of the Technical Institute and Experiment Station of Prague, recognzed as one of the leading authorities in the world on the difficult science of plant nutrition.

The old theory that plants build their food out of carbon dioxide which they capture from the air by means of their leaves, Dr. Stoklasa said, is entirely inadequate. The supplies of this gas in the air, according to his measurements, are not sufficient to account for the sugars, starches and other substances formed by plants with the assistance of the sun's energy. But the soil solution contains a great deal of carbon in the form of bicarbonates, and this carbon is taken into the plant along with the other soil minerals used by the plant, and borne by the sap to the green parts where carbohydrate manufacture is going on.

The amounts of carbon taken in from the soil, Prof. Stoklasa asserted, compare in quantity with the amounts of other minerals assimilated. Thus, for every hundred pounds of carbon so absorbed, 154 pounds of nitrogen, 113 pounds of phosphoric acid, 106 pounds of potash, 33 pounds of calcium oxide and 26 pounds of magnisum oxide are taken in. This indicates a hitherto little suspected and wholly unmeasured part played by carbon dioxide in the soil.

Of course not nearly all of the carbon dioxide given off by soil bacteria gets into the plants. A great deal of it escapes upwards, into the air. But here the leaves are waiting for it, and it passes into the plants through the channels hitherto taught as orthodox according to the accepted doctrines of plant physiology.

Furthermore, according to Prof. Stoklasa, fertilizers added to the soil are by no means entirely for the direct benefit of the corn or clover or other crops. A large share of these plant condiments fall to the share of the bacteria, stimulating them to greater activity in the production of materials eventually used in the production of foods by the higher plants.—*Science Service.*

Soil Bacteria and Poisons.—Small amounts of chemical substances in the soil, many of them poisonous to bacteria, seem to have a stimulating effect on these microscopic organisms as well as on the bigger plants whose lives they affect, according to Dr. J. E. Greaves, of the Utah Agricultural Experiment Station.

Discussing his studies on the rise and decline of soil bacterial populations before the First International Congress of Soil Sciences in session here this week, Dr. Greaves stated that he has found this stimulating effect followed the use of arsenic, of sodium sulphate and of sodium chloride, all of which are poisonous to bacteria in stronger concentrations.

The explanation which Dr. Greaves offers for this phenomenon is that the effect of the poisons is not a direct one. He inclines to the opinion that there is in the soil, along with the bacteria, a destructive substance or principle allied to the bacteriophage, prominent in recent medical research, and that the poisons cause increases or decreases in its activity, thereby causing the fluctuations in the number of bacteria.—*Science Service.*

SCIENTIFIC AND TECHNICAL ABSTRACTS

THE DETECTION OF LACTIC ACID IN PRESENCE OF OTHER ORGANIC ACIDS—It was suggested by the Revision Committee of the United States Pharmacopœia that an accurate chemical test be devised for the detection of alpha-hydroxypropionic acid, more familiarly known as lactic acid. An investigation was instituted, and the following facts presented herewith established:

Potassium thiocyanate, in solutions of 10 per cent. concentration, imparts to solutions of lactic acid of varying dilutions, alone or in presence of other salts of organic acids, a color that is not discharged by saturated solution of mercuric chloride. A number of soluble salts of organic acids were employed in the research, the acid ions representing: lactic, citric, tartaric, butyric, phosphoric, phosphorous, hypophosphorous, succinic, salicylic, benzoic, acetic, phenolsulphonic, and valeric acids.

As stated above, lactic acid alone or in the presence of the other organic acids, produced the color, which ranged from orange yellow to a purplish yellow in the more concentrated solutions employed in the experimental portion of the work.

It is believed that sulfonation, using the term in a broad sense, takes places in the $CH_3CHOHCOOH$ molecule, at the expense of the SCN radical of the potassium salt.

A number of reagents were employed tentatively prior to this, but without success. The results obtained by the use of the various chemical reagents is presented. Evidently, the reaction occurring is not of the metathetical type. It was at first believed that the coloration produced might be due to the presence of minute portions of $Fe+++$ ion. This view, however, was not borne out by subsequent tests, in which the color of undissociated $Fe(SCN)_3$ was eliminated by saturated solution of $HgCl_2$., while that due to the presence of $CH_3CHOHCOOH$ remained.

The adaptation of the procedure involved to quantitative methods will be considered for future employment.—*Jour. Ind. & Eng. Chem.*, July, 1927.

Artificial Ripening of Fruits and Vegetables.—In the past, ethylene has been used for coloring citrus fruits and by its use it has been possible to make green fruit appear ripe, which was none too proper. However, Dr. Harvey has found that by continued application of either ethylene or propylene, an actually green fruit can be made to undergo exactly the same changes in composition that occur in ripening on the plant.

It is useful in removing excess acidity from early apples, plums, rhubarb, pineapples, and other fruits. It will produce better flavor in musk, honey-dew, and casaba melons. Of the tropical fruits, we may now hope to have a greater share available in the north. The mango, avocado, papaya, custard apple, chayote, jujube, and persimmon offer commercial possibilities since they may now be shipped in a firm green condition.

Ethylene is the most practical gas for use in ripening, although propylene is a little more active and produces a little better flavor in fruits. Propylene is not available commercially at present. Acetylene is considerably more toxic than ethylene or propylene and has an unpleasant odor in the commercially available product. Ethylene can be obtained in cylinders.

Ethylene may be used to remove the excess acidity of fruits or vegetables, to remove chlorophyll from celery or similar plants, to increase the sugar content, or to remove tannins and other objectionable substances. Tomatoes ripened after removal from the vine in winter are liable to be excessively acid, but if treated with ethylene they have a fine flavor, free from excess acidity. Very immature tomatoes down to one inch in

diameter may be ripened in six to eight days; more mature fruits require only twenty-four to sixty hours, depending upon the variety and degree of maturity. It is practicable to ripen two-third or three-fourths size tomatoes for the market at times of high prices. Tomatoes have better flavor when so ripened than those ripened on the vine. This will make it possible to extend the length of the season by ripening immature fruits before the regular season, and also will save fruits caught green by frost.

Celery can be blanched perfectly in sixty hours and has a fine color, sweeter taste, and less stringiness. A single does of ethylene, about two to three cubic feet, costing less than forty cents per carload of fruit, is sufficient to produce a remarkable change in the time required to ripen bananas, and to change their color, flavor, and texture to that of fine, ripe fruit. The tannins of the date and of the Japanese persimmon have been more quickly removed than is possible without ethylene. The astringent Japanese persimmons were nicely ripened in fifty hours with ethylene while controls at the same temperature were still very astringent. Ethylene causes a sudden jump in the respiratory rate after its application. Attendant with this increased rate of respiration, the fruit acids and tannins disappear.—*Scientific American,* July, 1927, p. 74.

NEWS ITEMS AND PERSONAL NOTES

COMPLIMENTARY DINNER IN PHILADELPHIA TO DR. ROBERT J. RUTH—Dr. Robert J. Ruth, who has so efficiently represented the Philadelphia College of Pharmacy and Science as its Field Secretary during the past three years, was given an honorable dismissal in May by the Board of Trustees of the Institution, who passed resolutions commending his loyalty and his work.

Dr. Ruth has since joined the staff of E. R. Squibb & Sons, of New York. In view of his approaching departure from Philadelphia early in July, more than thirty of his friends in Philadelphia tendered Dr. and Mrs. Ruth a dinner in the Red Room of the Bellevue-Stratford Hotel on the evening of Wednesday, June 29th.

The following is the list of guests who were present:

Mr. and Mrs. Wilmer Krusen, Mr. and Mrs. Josiah C. Peacock, Professor Freeman P. Stroup, Professor Horatio C. Wood, Dr. F. E. Stewart, Mr. W. W. McNeary, Professor and Mrs. Marin S. Dunn, Professor and Mrs. Charles H. LaWall, Professor and Mrs. E. Fullerton Cook, Mr. and Mrs. J. W. E. Harrisson, Professor and Mrs. J. W. Sturmer, Professor and Mrs. Frank X. Moerk, Professor Ivor Griffith, Dr. Leo G. Penn, Professor Arno Viehoever, Professor L. Gershenfeld, Dr. W. Duffield Robinson, Mr. Brua C. Goodhart, Mr. Raymond Hendrickson, Mr. and Mrs. John C. Eckel, Mr. and Mrs. Ambrose Hunsberger and Ambrose Hunsberger, Jr.

Several hours were spent in pleasant social intercourse and complimentary remarks concerning Dr. Ruth's work were made by a number of those who were present.

Special guests from the Squibb staff in New York were present. These were Mr. Lewis H. Davis, Editor of "Squibbs Message," and Mr. Dunlap, Director of Sales Force of the Eastern United States.

THE EDITOR OF THE JOURNAL VACATIONING IN EUROPE—Professor Ivor Griffith, with his wife and daughter, are now riding the high seas on their way to Europe, where they have planned an extensive tour. The native heather is their first objective—whence, after the non-Welsh members of the family will have used up their patience; the trio will tour England, France, Italy—and some other countries smaller and much less important than Wales.

The Journal wishes the trio a happy voyage—a pleasant sojourn and a safe return.

HEADQUARTERS BUILDING OF THE A. PH. A. FINALLY LOCATED—The last vote of the membership of the American Pharmaceutical Association has been counted, and as a result the new Headquarters Building will be located at Washington, D. C.

To which we react that the members voted wisely—and well.

BOOK REVIEWS

SADTLER, COBLENTZ AND HOSTMANN'S PHARMACEUTICAL AND MEDICAL CHEMISTRY. Sixth Edition. Revised and rewritten by Freeman P. Stroup, Ph.M. Octavo. 709 pages. Cloth binding. Price $7. J. B. Lippincott Company, Publishers, Philadelphia.

In no branch of science has the modern spirit of research wrought greater changes within a decade than in chemistry. The volume before us, although named "Pharmaceutical and Medical Chemistry" has in all of its editions endeavored to teach chemistry as well as to lay emphasis on the pharmaceutical and medical applications of that science. It is a difficult matter, with the with the tremendous growth of our knowledge of "pure chemistry," to strike a proper balance, for the student of pharmacy and medicine between what he ought to know of chemistry in the abstract and what will be of direct use to him in his profession.

To those who believe that anyone using chemistry in his profession should first be given a complete course in that science without emphasis on its application, this volume will probably seem inadequate. This is not necessarily a fault. It is merely what must be expected whenever one tries to combine the "pure" and the "applied" in one volume and keeps the volume reasonably small.

The service rendered by this volume—and it is a very great service—is two fold.

First, it supplements the books and courses in chemistry which are free of pharmaceutical and medical application.

Secondly, it fills the need for a text in the many instances where teachers of chemistry in pharmacy and medical schools prefer an applied text, which they supplement in their lectures with the more extended theoretical considerations.

Both systems of teaching are in vogue and there is much to be said in favor of each.

The organic portion of the text bears the marks of complete revision. The inorganic portion has not received quite the same treatment. One cannot fail to notice the very gradual absorption of the newer concepts and the similarly slow elimination of the old. This volume seems to stand between the very old and the very new, and in that position it has another sphere

of usefulness. Those who prepare for State Board examinations and wish to review their chemistry are apt to be safer in their study with a book like this than with one of the late editions on General Chemistry by recent authors.

The chapters cover General Chemistry and Chemical Theory; Hydrogen; the Halogens; the Oxygen Group; the Nitrogen Group; Boron; the Carbon Group; Classification of the Elements; the Alkali Metals; the Alkali-Earth Group; the Magnesium Group; the Silver Group; the Copper and Mercury Group; the Earth-Metal Group; the Tin Group; the Chromium Group; the Iron Group; the Platinum Group; Chemistry of the Organic Componds; Open-Chain (A-Cyclic) Hydrocarbons; Derivatives of the Open-Chain Hydrocarbons; Closed-Chain or Cyclic Compounds; Isocyclic Compounds containing One Nucleus; Aromatic Compounds with more than One Nucleus; Heterocyclic Compounds; the Alkaloids and Ptomaines; the Terpenes and their Derivatives; Glucosides—Bitter and Neutral Principles; Tissue-forming substances, proteins; Electrolysis and its applications; and Strengths of Acid and Alkalies.

The book considers particularly the chemicals of the U. S. P. X, the N. F. V, and many of those of the N. N. R., 1926. In the Organic section much valuable material is arranged in tabular form so as to be more accessible for quick reference. Over seven thousand references are contained in the very complete index.

Pharmacists who wish to keep their libraries up-to-date should add this edition to their shelves, particularly if they limit their books on chemistry to one volume.

ROBERT P. FISCHELIS.

DIE ROHSTOFFE DES PFLANZENREICHES. By Julius von Wiesner, with assistance of collaborators. 1st volume, Alkaloids to Yeasts. 8vo., iv-1122 pages, 307 illustrations. 4th edition. Paul Krais, Dresden, and Wilhelm von Brehmer, Berlin-Dahlem. Sewed, 46 marks; bound, 49 marks.

The earlier issues of the data to which this work is devoted appeared in a series of more or less disconnected monographs. It was regarded as more satisfactory to bring together the large amount of information available not according to the applications but accord-

ing to the sources, that is, whether from root, leaves, stems, fruits, etc. The author has had full aid from his collaborators and the result is an immense amount of information on the sources, properties and composition of the raw materials yielded by the vegetable kingdom. Plants are the intermediaries between animal life and the inorganic constituents of the soil. They yield us nourishment directly and indirectly and they yield medicines. They are by no means all beneficent. Nature seems to be indifferent to her creations in many ways, for while furnishing a vast amount of products which contribute to pleasure, nature also sprinkles our path with dangerous forms. As we stroll along the road or through the field or forest we have frequent occasion to admire the beauty of the flowers and plant forms and to rejoice in the nutritious and delectable fruits, but we are often disillusioned by the sight of poison ivy or worthless weeds such as the Ambrosias.

As noted above, this volume covers only part of the subject, and as the topics are arranged in the order of the alphabet, covering from A to H (Alkaloide bis Hefen), it seems likely that two more at least will be required to complete the work. The individual topics and their contributors are as follows, the apparent lack of alphabetical relation being due to the difference of terms in the German and English:

Introduction by J. Wiesner, revised by P. Krais and W. v. Brehmer.
Alkaloids, by F. Boas.
Ethereal Oils and Camphor, by K. Bournot. Botanical part by E. Gilg and P. N. Schurhoff.
Bitter Substances, by J. Messner.
Albuminoids, by F. Boas.
Colors, by R. Hofmann. Botanical part by Gilg and Schurhoff.
Fibers and Basts, by J. Weese. Chemical part by S. Zeisel.
Fats and Oils, by H. Wolff, assisted by A. Müller.
Tanning Materials, by W. v. Brehmer. Chemical part by Zeisel.
Galls, by W. Figdor.
Gums, by Brehmer. Chemical part by Zeisel.
Resins and Balsams, by H. Wolff.
Yeasts, by F. Boas.

After each section a comprehensive bibliography is given, references to which are found in the text. This bibliography is alone

sufficient to show the industry and thoroughness with which the literature has been searched. The most extensive section is on fibers and basts, covering over three hundred pages, liberally illustrated with excellent drawings. The chapter includes a valuable and interesting account of the fibers used for paper, with illustration of the structure and method of use of the papyrus plant which has had so important a role in early literature. In this connection the use of certain portions of birch bark for manuscript is mentioned, and a photograph is given of a portion of an ancient MS. of this nature containing characters somewhat similar to those of Sanskrit.

Each article is so comprehensive and so full of information, aided whenever possible by excellent illustrations, that a reading of it will place one in possession of all the important data. The book is really a collection of textbooks each written by a specialist, and when the series is completed little if any of our present knowledge on the subject of plant products will be lacking.

Of course one notes the now unfortunate tendency of German scientists to substitute terms from their own language for standard international terms. In this mood "stomata" of most botanists is replaced by "Spaltoefnungen." Such cases are as yet rare, and the book will be a most acceptable addition to the library of the plant chemist and pharmacologist.

HENRY LEFFMANN.